

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

United States Patent and Trademark
Office
(Box PCT)
Crystal Plaza 2
Washington, DC 20231
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 25 May 1998 (25.05.98)	Applicant's or agent's file reference 5500-01-TMC
International application No. PCT/US97/18514	Priority date (day/month/year) 11 October 1996 (11.10.96)
International filing date (day/month/year) 09 October 1997 (09.10.97)	Applicant ALBRECHT, Hans, P. et al

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:
30 April 1998 (30.04.98)

☐ in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was
☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer A. Addae-Ruesch Telephone No.: (41-22) 338.83.38
---	--

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav Republic of Macedonia	TM	Turkmenistan
BF	Burkina Faso	GR	Greece			TR	Turkey
BG	Bulgaria	HU	Hungary	ML	Mali	TT	Trinidad and Tobago
BJ	Benin	IE	Ireland	MN	Mongolia	UA	Ukraine
BR	Brazil	IL	Israel	MR	Mauritania	UG	Uganda
BY	Belarus	IS	Iceland	MW	Malawi	US	United States of America
CA	Canada	IT	Italy	MX	Mexico	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NE	Niger	VN	Viet Nam
CG	Congo	KE	Kenya	NL	Netherlands	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NO	Norway	ZW	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's Republic of Korea	NZ	New Zealand		
CM	Cameroon			PL	Poland		
CN	China	KR	Republic of Korea	PT	Portugal		
CU	Cuba	KZ	Kazakhstan	RO	Romania		
CZ	Czech Republic	LC	Saint Lucia	RU	Russian Federation		
DE	Germany	LI	Liechtenstein	SD	Sudan		
DK	Denmark	LK	Sri Lanka	SE	Sweden		
EE	Estonia	LR	Liberia	SG	Singapore		

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 97/18514

A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 C07C271/22 C07C233/47 C07C233/51 C07C311/19 C07D333/24

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 C07C C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 618 223 A (SANDOZ) 5 October 1994 see claims 1,10; example 31 ---	1,30
X	ADNAN M.M. MJALLI ET AL : "Inhibition of interleukin-1beta converting enzyme by N-acyl-aspartic acid ketones" BIOORGANIC & MEDICINAL CHEMISTRY LETTERS, vol. 5, no. 13, 1995, pages 1405-1408, XP002053982 see page 1405; examples 3J-N ---	1,30
X	ADNAN M.M. MJALLI ET AL: "Activated ketones as potent reversible inhibitors of interleukin-1beta converting enzyme" BIOORGANIC & MEDICINAL CHEMISTRY LETTERS, vol. 4, no. 16, 1994, pages 1965-1968, XP002054017 see page 1965; example 4C ---	1,30
-/-		

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

30 January 1998

Date of mailing of the international search report

19. 02. 98

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Voyiazoglou, D

INTERNATIONAL SEARCH REPORT

International Application No.

PCT/US 97/18514

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
----------	--	-----------------------

A

EP 0 623 592 A (STERLING) 9 November 1994
see claims 1,3

1,30,43

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 97/18514

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 21-29
because they relate to subject matter not required to be searched by this Authority, namely:
Remark: Although claim(s) 21-29
is(are) directed to a method of treatment of the human/animal
body, the search has been carried out and based on the alleged
effects of the compound/composition.
2. ☒ Claims Nos.: 1-18, 20, 30
because they relate to parts of the International Application that do not comply with the prescribed requirements to such
an extent that no meaningful International Search can be carried out, specifically:
The claims are so broad that to determining the scope of a meaningful
search due account has been taken of Rule 33.3 PCT, special emphasis was
put on the subject matter of claims 19, 31-40, 43
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all
searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment
of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report
covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is
restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 97/18514

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 618223 A	05-10-94	CA 2117121 A	09-09-94
		JP 6340691 A	13-12-94
EP 623592 A	09-11-94	AU 676887 B	27-03-97
		AU 6075294 A	03-11-94
		CA 2122227 A	30-10-94
		CZ 9401035 A	16-11-94
		FI 942005 A	30-10-94
		HU 68563 A	28-06-95
		JP 7025865 A	27-01-95
		NO 941580 A	31-10-94
		NZ 260410 A	25-06-96
		SK 50294 A	08-02-95



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁶ : C07C 271/22, 233/47, 233/51, 311/19, C07D 333/24	A1	(11) International Publication Number: WO 98/16502 (43) International Publication Date: 23 April 1998 (23.04.98)
--	----	--

(21) International Application Number: PCT/US97/18514
(22) International Filing Date: 9 October 1997 (09.10.97)

(30) Priority Data:
60/028,322 11 October 1996 (11.10.96) US

(71) Applicant (for all designated States except US):
WARNER-LAMBERT COMPANY [US/US]; 201
Tabor Road, Morris Plains, NJ 07950 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): ALBRECHT, Hans, P.
[DE/DE]; Am Wetzelsberg 59, D-69517 Gornheimertal
(DE). ALLEN, Hamish, John [GB/US]; 47 Eastern Point
Drive, Shrewsbury, MA 01545 (US). BRADY, Kenneth,
Dale [US/US]; 32 Ivernia Road, Worcester, MA 01606
(US). CAPRATHE, Bradley, William [US/US]; 31480
Myma, Livonia, MI 48154 (US). GILMORE, John, Lodge
[US/US]; Apartment 178C, 3695 Greenbrier Boulevard, Ann
Arbor, MI 48105 (US). HARTER, William, Glen [US/US];
3750 Shagbark, Chelsea, MI 48118 (US). HAYS, Sheryl,
Jeanne [US/US]; 2729 Aspen Road, Ann Arbor, MI 48108
(US). KOSTLAN, Catherine, Rose [US/US]; 9876 Moon
Road, Saline, MI 48176 (US). LUNNEY, Elizabeth, Ann
[US/US]; 619 Ridgewood Court, Ann Arbor, MI 48103

(US). PARA, Kimberly, Suzanne [US/US]; 2735 Dexter
Avenue, Ann Arbor, MI 48103 (US). THOMAS, Anthony,
Jerome [US/US]; 2909 Brockman, Ann Arbor, MI 48104
(US). WALKER, Nigel [GB/DE]; Frauenpfad 20, D-69221
Dossenheim (DE).

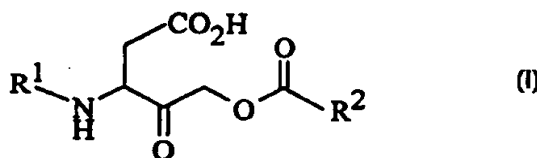
(74) Agents: RYAN, M., Andrea; Warner-Lambert Company, 201
Tabor Road, Morris Plains, NJ 07950 (US) et al.

(81) Designated States: AL, AU, BA, BB, BG, BR, CA, CN, CZ,
EE, GE, HU, ID, IL, IS, JP, KR, LC, LK, LR, LT, LV, MG,
MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT,
UA, US, UZ, VN, YU, ARIPO patent (GH, KE, LS, MW,
SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ,
MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK,
ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI
patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN,
TD, TG).

Published

*With international search report.
Before the expiration of the time limit for amending the
claims and to be republished in the event of the receipt of
amendments.*

(54) Title: ASPARTATE ESTER INHIBITORS OF INTERLEUKIN-1 β CONVERTING ENZYME



(57) Abstract

The present invention relates to compounds that are inhibitors of interleukin-1 β converting enzyme that have formula (I). This invention also relates to a method of treatment of stroke, inflammatory diseases, reperfusion injury, Alzheimer's disease, and shigellosis, and to a pharmaceutically acceptable composition that contains a compound that is an inhibitor of interleukin-1 β converting enzyme.

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 5500-01-TMC	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/US 97/ 18514	International filing date (day/month/year) 09/10/1997	(Earliest) Priority Date (day/month/year) 11/10/1996
Applicant WARNER-LAMBERT COMPANY et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 4 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. ☒ Certain claims were found unsearchable (see Box I).

2. ☐ Unity of invention is lacking (see Box II).

3. ☐ The international application contains disclosure of a nucleotide and/or amino acid sequence listing and the international search was carried out on the basis of the sequence listing

☐ filed with the international application.

☐ furnished by the applicant separately from the international application,

☐ but not accompanied by a statement to the effect that it did not include matter going beyond the disclosure in the international application as filed.

☐ Transcribed by this Authority

4. With regard to the title, ☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the abstract,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this International Search Report, submit comments to this Authority.

6. The figure of the drawings to be published with the abstract is:

Figure No. --- ☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☐ None of the figures.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 97/ 18514

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 21-29
because they relate to subject matter not required to be searched by this Authority, namely:
Remark: Although claim(s) 21-29
is(are) directed to a method of treatment of the human/animal
body, the search has been carried out and based on the alleged
effects of the compound/composition.
2. ☒ Claims Nos.: 1-18, 20, 30
because they relate to parts of the International Application that do not comply with the prescribed requirements to such
an extent that no meaningful International Search can be carried out, specifically:
The claims are so broad that to determining the scope of a meaningful
search due account has been taken of Rule 33.3 PCT, special emphasis was
put on the subject matter of claims 19, 31-40, 43
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all
searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment
of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report
covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is
restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 97/18514

A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 C07C271/22 C07C233/47 C07C233/51 C07C311/19 C07D333/24

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 C07C C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 618 223 A (SANDOZ) 5 October 1994 see claims 1,10; example 31 ---	1,30
X	ADNAN M.M. MJALLI ET AL : "Inhibition of interleukin-1beta converting enzyme by N-acyl-aspartic acid ketones" BIOORGANIC & MEDICINAL CHEMISTRY LETTERS, vol. 5, no. 13, 1995, pages 1405-1408, XP002053982 see page 1405; examples 3J-N ---	1,30
X	ADNAN M.M. MJALLI ET AL: "Activated ketones as potent reversible inhibitors of interleukin-1beta converting enzyme" BIOORGANIC & MEDICINAL CHEMISTRY LETTERS, vol. 4, no. 16, 1994, pages 1965-1968, XP002054017 see page 1965; example 4C ---	1,30

-/--



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

30 January 1998

Date of mailing of the international search report

19. 02. 98

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Voyiazoglou, D

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 97/18514

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>EP 0 623 592 A (STERLING) 9 November 1994 see claims 1,3</p> <p>-----</p>	<p>1,30,43</p>

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 97/18514

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 618223 A	05-10-94	CA 2117121 A JP 6340691 A	09-09-94 13-12-94
EP 623592 A	09-11-94	AU 676887 B AU 6075294 A CA 2122227 A CZ 9401035 A FI 942005 A HU 68563 A JP 7025865 A NO 941580 A NZ 260410 A SK 50294 A	27-03-97 03-11-94 30-10-94 16-11-94 30-10-94 28-06-95 27-01-95 31-10-94 25-06-96 08-02-95